

Amendment to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

1-38. (Canceled)

39. (Currently amended) ~~The composition of claim 1, wherein:~~ A composition comprising:
an siRNA or shRNA molecule targeted to a transcript of a respiratory virus, which molecule comprises
(a) a first single-stranded RNA molecule consisting of a sequence that is homologous to highly conserved region of the target transcript among a plurality of variants of the virus and comprises at least 15 consecutive nucleotides,
(b) a second single-stranded molecule that comprises a region that is complementary to the first strand, and
(c) an RNA duplex formed by the first and second RNA molecules hybridizing together,
wherein the siRNA or shRNA molecule inhibits production of the virus by at least 2 fold, relative to the level that would be present in the absence of the siRNA or shRNA molecule, in cells infected by the virus; and
wherein the first strand comprises at least 10 consecutive nucleotides as set forth in nucleotides 3 through 21 of the sequence presented in any of SEQ ID NOS: 1 through 68.
40. (Currently amended) ~~The composition of claim 1—claim 39,~~ wherein:
the first strand comprises at least 12 consecutive nucleotides as set forth in nucleotides 3 through 21 of the sequence presented in any of SEQ ID NOS: 1 through 68.
41. (Currently amended) ~~The composition of claim 1—claim 39,~~ wherein:
the first strand comprises at least 15 consecutive nucleotides as set forth in nucleotides 3 through 21 of the sequence presented in any of SEQ ID NOS: 1 through 68.

42. (Currently amended) The composition of ~~claim 1~~ claim 39, wherein:
the first strand comprises at least 17 consecutive nucleotides as set forth in nucleotides 3 through 21 of the sequence presented in any of SEQ ID NOS: 1 through 68.
43. (Currently amended) The composition of ~~claim 1~~ claim 39, wherein:
the first strand comprises at least 19 consecutive nucleotides as set forth in nucleotides 3 through 21 of the sequence presented in any of SEQ ID NOS: 1 through 68.
44. (Currently amended) ~~The composition of claim 1, wherein:~~ A composition comprising:
an siRNA or shRNA molecule targeted to a transcript of a respiratory virus, which molecule comprises
(a) a first single-stranded RNA molecule consisting of a sequence that is homologous to highly conserved region of the target transcript among a plurality of variants of the virus and comprises at least 15 consecutive nucleotides,
(b) a second single-stranded molecule that comprises a region that is complementary to the first strand, and
(c) an RNA duplex formed by the first and second RNA molecules hybridizing together,
wherein the siRNA or shRNA molecule inhibits production of the virus by at least 2 fold, relative to the level that would be present in the absence of the siRNA or shRNA molecule, in cells infected by the virus; and
wherein the first strand comprises at least 10 consecutive nucleotides as set forth in nucleotides 3 through 21 of the sequence presented in any of SEQ ID NOS: 1 through 68, with the proviso that either one or two nucleotides among the 10 consecutive nucleotides may differ from that sequence.
45. (Currently amended) The composition of ~~claim 1~~ claim 44, wherein:
the first strand comprises at least 12 consecutive nucleotides as set forth in nucleotides 3 through 21 of the sequence presented in any of SEQ ID NOS: 1 through 68, with the proviso that either one or two nucleotides among the 12 consecutive nucleotides may differ from that sequence.

46. (Currently amended) The composition of ~~claim 1~~claim 44, wherein:
the first strand comprises at least 15 consecutive nucleotides as set forth in nucleotides 3 through 21 of the sequence presented in any of SEQ ID NOS: 1 through 68, with the proviso that either one or two nucleotides among the 15 consecutive nucleotides may differ from that sequence.
47. (Currently amended) The composition of ~~claim 1~~claim 44, wherein:
the first strand comprises at least 17 consecutive nucleotides as set forth in nucleotides 3 through 21 of the sequence presented in any of SEQ ID NOS: 1 through 68, with the proviso that either one or two nucleotides among the 17 consecutive nucleotides may differ from that sequence.
48. (Currently amended) The composition of ~~claim 1~~claim 44, wherein:
the first strand comprises at least 19 consecutive nucleotides as set forth in nucleotides 3 through 21 of the sequence presented in any of SEQ ID NOS: 1 through 68, with the proviso that either one or two nucleotides among the 19 consecutive nucleotides may differ from that sequence.
- 49-63. (Canceled)
64. (Currently amended) ~~The composition of claim 1, wherein:~~ A composition comprising:
an siRNA or shRNA molecule targeted to a transcript of a respiratory virus, which molecule comprises
(a) a first single-stranded RNA molecule consisting of a sequence that is homologous to highly conserved region of the target transcript among a plurality of variants of the virus and comprises at least 15 consecutive nucleotides,
(b) a second singled-stranded molecule that comprises a region that is complementary to the first strand, and
(c) an RNA duplex formed by the first and second RNA molecules hybridizing together,
wherein the siRNA or shRNA molecule inhibits production of the virus by at least 2 fold, relative to the level that would be present in the absence of the siRNA or shRNA molecule, in cells infected by the virus; and

wherein the duplex comprises sequences given by nucleotides 1 – 19 of SEQ ID NOS: 93 and 94 respectively, with, optionally, a 3' overhang on one or both sequences.

65. (Currently amended) ~~The composition of claim 1, wherein:~~ A composition comprising:
an siRNA or shRNA molecule targeted to a transcript of a respiratory virus, which
molecule comprises

(a) a first single-stranded RNA molecule consisting of a sequence that is
homologous to highly conserved region of the target transcript among a plurality of
variants of the virus and comprises at least 15 consecutive nucleotides,

(b) a second single-stranded molecule that comprises a region that is
complementary to the first strand, and

(c) an RNA duplex formed by the first and second RNA molecules hybridizing
together,

wherein the siRNA or shRNA molecule inhibits production of the virus by at least
2 fold, relative to the level that would be present in the absence of the siRNA or shRNA
molecule, in cells infected by the virus; and

wherein the duplex comprises sequences given by nucleotides 1 – 20 of SEQ ID NOS: 188 and 189 respectively, with, optionally, a 3' overhang on one or both sequences.

66. (Currently amended) ~~The composition of claim 1, wherein:~~ A composition comprising:
an siRNA or shRNA molecule targeted to a transcript of a respiratory virus, which
molecule comprises

(a) a first single-stranded RNA molecule consisting of a sequence that is
homologous to highly conserved region of the target transcript among a plurality of
variants of the virus and comprises at least 15 consecutive nucleotides,

(b) a second single-stranded molecule that comprises a region that is
complementary to the first strand, and

(c) an RNA duplex formed by the first and second RNA molecules hybridizing
together,

wherein the siRNA or shRNA molecule inhibits production of the virus by at least
2 fold, relative to the level that would be present in the absence of the siRNA or shRNA
molecule, in cells infected by the virus; and

wherein the siRNA or shRNA duplex is selected from the group consisting of duplex portions of: NP-1496, NP-1496a, PA-2087, PB1-2257, PB1-129, PB2-2240, M-37, or M-598 or a variant of any of the foregoing, which variant differs by at most one nucleotide from the corresponding siRNA.

67. (Previously presented) The composition of claim 66, wherein the siRNA or shRNA duplex is identical to the duplex portion of NP-1496.
68. (Previously presented) The composition of claim 66, wherein the siRNA or shRNA duplex is identical to the duplex portion of NP-1496a.
69. (Currently amended) ~~The composition of claim 1, wherein:~~ A composition comprising:
an siRNA or shRNA molecule targeted to a transcript of a respiratory virus, which molecule comprises
(a) a first single-stranded RNA molecule consisting of a sequence that is homologous to highly conserved region of the target transcript among a plurality of variants of the virus and comprises at least 15 consecutive nucleotides,
(b) a second single-stranded molecule that comprises a region that is complementary to the first strand, and
(c) an RNA duplex formed by the first and second RNA molecules hybridizing together,
wherein the siRNA or shRNA molecule inhibits production of the virus by at least 2 fold, relative to the level that would be present in the absence of the siRNA or shRNA molecule, in cells infected by the virus; and
wherein the first strand has a sequence selected from the group consisting of: the first 19 nucleotides of SEQ ID NO: 71, SEQ ID NO: 75, SEQ ID NO: 77, SEQ ID NO: 83, SEQ ID NO: 93; SEQ ID NO: 95; SEQ ID NO: 99, and SEQ ID NO: 188, reading in a 5' to 3' direction.

70-93. (Canceled)

94. (Currently amended) ~~The vector of claim 92,~~ A vector comprising a nucleic acid that encodes an siRNA or shRNA molecule that is targeted to a transcript of a respiratory

virus, which molecule comprises

(a) a first single-stranded RNA molecule consisting of a sequence that is homologous to highly conserved region of the target transcript among a plurality of variants of the virus and comprises at least 15 consecutive nucleotides,

(b) a second single-stranded molecule that comprises a region that is complementary to the first strand, and

(c) an RNA duplex formed by the first and second RNA molecules hybridizing together,

wherein the siRNA or shRNA molecule inhibits production of the virus by at least 2 fold, relative to the level that would be present in the absence of the siRNA or shRNA molecule, in cells infected by the virus;

wherein multiple variants of the virus exist and wherein the virus is capable of undergoing genetic reassortment or mixing;

wherein the respiratory virus is an influenza virus;

wherein the siRNA or shRNA molecule reduces susceptibility of the cell to infection by influenza virus or inhibits influenza virus production; and

wherein the sequence of the first strand of the siRNA or shRNA molecule is selected from the group consisting of: NP-1496, NP-1496a, PA-2087, PB1-2257, PB1-129, PB2-2240, M-37, and M-598, or a variant of any of the foregoing, wherein the variant differs by at most one nucleotide from the sequence.

95. (Previously presented) The vector of claim 94, wherein the sequence of the first strand of the siRNA or shRNA molecule is identical to NP-1496.
96. (Previously presented) The vector of claim 94, wherein the sequence of the first strand of the siRNA or shRNA molecule is identical to NP-1496a.
97. (Previously presented) The vector of claim 94, wherein the first strand of the siRNA or shRNA molecule has a sequence selected from the group consisting of: the first 19 nucleotides of any of SEQ ID NOS: 71, 75, 77, 83, 93, 95, 99, and 188, reading in a 5' to 3' direction.
- 98-178.

179. (Currently amended) ~~The composition of claim 165, wherein:~~ A composition comprising:
an siRNA or shRNA molecule, wherein the molecule is targeted to an influenza virus transcript, which molecule comprises
(a) a first single-stranded RNA molecule consisting of a sequence that is homologous to highly conserved region of the target transcript among a plurality of variants of the virus and comprises at least 15 consecutive nucleotides,
(b) a second singled-stranded molecule that comprises a region that is complementary to the first strand, and
(c) an RNA duplex formed by the first and second RNA molecules hybridizing together,
wherein the siRNA or shRNA molecule inhibits production of the virus by at least 2 fold, relative to the level that would be present in the absence of the siRNA or shRNA molecule, in cells infected by the virus; and
a delivery agent selected from the group consisting of: cationic polymers, modified cationic polymers, peptide molecular transporters, surfactants suitable for introduction into the lung, neutral or cationic lipids, liposomes, non-cationic polymers, modified non-cationic polymers, bupivacaine, and chloroquine; and
wherein the sequence of the first strand of the siRNA or shRNA comprises a sequence-selected from the group consisting of: NP-1496, NP-1496a, PA-2087, PB1-2257, PB1-129, PB2-2240, M-37, and M-598, or a variant of any of the foregoing, wherein the variant sequence differs by at most one nucleotide from the corresponding sequence of the first strand.
180. (Previously presented) The composition of claim 179, wherein the first strand sequence comprises NP-1496.
181. (Previously presented) The composition of claim 179, wherein the first strand sequence comprises NP-1496a.
182. (Currently amended) ~~The composition of claim 165, wherein:~~ A composition comprising:

an siRNA or shRNA molecule, wherein the molecule is targeted to an influenza virus transcript, which molecule comprises

(a) a first single-stranded RNA molecule consisting of a sequence that is homologous to highly conserved region of the target transcript among a plurality of variants of the virus and comprises at least 15 consecutive nucleotides,

(b) a second single-stranded molecule that comprises a region that is complementary to the first strand, and

(c) an RNA duplex formed by the first and second RNA molecules hybridizing together,

wherein the siRNA or shRNA molecule inhibits production of the virus by at least 2 fold, relative to the level that would be present in the absence of the siRNA or shRNA molecule, in cells infected by the virus; and

wherein the sequence of the first strand comprises a sequence selected from the group consisting of: the first 19 nucleotides of, SEQ ID NO: 71, SEQ ID NO: 75, SEQ ID NO: 77, SEQ ID NO: 83, SEQ ID NO: 93; SEQ ID NO: 95; SEQ ID NO: 99, and SEQ ID NO: 188 reading in a 5' to 3' direction.

183. (Previously presented) The composition of claim 182, wherein the sequence of the first strand comprises the sequence of SEQ ID NO: 93.

184. (Previously presented) The composition of claim 182, wherein the sequence of the first strand comprises the sequence of SEQ ID NO: 188.

185-200 (Canceled)

201. (Previously presented) A composition comprising:

an siRNA or shRNA targeted to a target transcript of an influenza NP gene, wherein the siRNA or shRNA comprises a core duplex region having sense and antisense strands or portions, wherein the sequence of the sense strand or portion of the core duplex region comprises at least 10 consecutive nucleotides of a target sequence selected from the group consisting of:

nucleotides 3 – 21 of a sequence presented in any of SEQ ID NOs: 1 through 68, with the proviso that either one or two nucleotides among the 19 consecutive nucleotides

may differ from that sequence;

nucleotides 1 – 19 of SEQ ID NO: 93, with, optionally, a 3' overhang;

nucleotides 1 – 20 of SEQ ID NO: 188, with, optionally, a 3' overhang; and

nucleotides 1 – 19 of SEQ ID NOs: 93 or 188.